check for patents

L3 ANSWER 1 OF 49 MEDLINE
ACCESSION NUMBER: 2003049505 IN-PROCESS
DOCUMENT NUMBER: 22446456 PubMed ID: 12393532
TITLE: **Rapamycin** specifically interferes with GM-CSF signaling in human **dendritic** cells, leading to apoptosis via increased p27KIP1 expression.
AUTHOR: Woltman Andrea M; Van Der Kooij Sandra W; Coffer Paul J; Offringa Rienk; Daha Mohamed R; Van Kooten Cees
CORPORATE SOURCE: Department of Nephrology and Department of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands; Department of Pulmonary Diseases, University Medical Center Utrecht, Utrecht, The Netherlands.
SOURCE: BLOOD, (2003 Feb 15) 101 (4) 1439-45. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Abridged Index Medicus Journals; Priority Journals
ENTRY DATE: Entered STN: 20030202
Last Updated on STN: 20030202

AB The longevity of **dendritic** cells (DCs) is a critical regulatory factor influencing the outcome of immune responses. Recently, we demonstrated that the immunosuppressive drug **rapamycin** (Rapa) specifically induces apoptosis in DCs but not in other myeloid cell types.

The present study unraveled the mechanism used by Rapa to induce apoptosis in human monocyte-derived DCs. Our data demonstrate that granulocyte-macrophage colony-stimulating factor (GM-CSF) preserves DC survival specifically via the phosphatidylinositol-3 lipid kinase/mammalian target of **rapamycin** (PI3K/mTOR) signaling pathway, which is abrogated by Rapa at the level of mTOR. Disruption of this GM-CSF signaling pathway induced loss of mitochondrial membrane potential, phosphatidyl-serine exposure, and nuclear changes. Apoptosis of these nonproliferating DCs was preceded by an up-regulation of the cell cycle inhibitor p27(KIP1). Overexpression of p27(KIP1) in DCs using adenoviral gene transduction revealed that apoptosis is directly regulated by p27(KIP1). Furthermore, both overexpression of p27(KIP1) and disruption of the GM-CSF/PI3K/mTOR signaling pathway decreased the expression of the antiapoptotic protein mcl-1. This mTOR/p27(KIP1)/mcl-1 survival seems unique for DCs and may provide novel opportunities to influence immune responses by specific interference with the life span of these cells.

L3 ANSWER 2 OF 49 MEDLINE DUPLICATE 1